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REMARKS

Sequence Listing

The Examiner indicated that the subject application does not comply with the requirements of 37 C.F.R. §§1.821-1.825 for the reasons set forth on the Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures that was enclosed with the August 13, 2003 Office Action. A copy of the Notice is attached hereto as **Exhibit 2**.

Applicants have hereinabove amended the specification to provide a Sequence Listing for the nucleotide sequences (primers) set forth on pages 50-52 of the application. Applicants maintain that the amendments to the specification do not raise an issue of new matter. Accordingly, applicants respectfully request that the amendments be entered.

A paper copy of a Sequence Listing is provided as **Exhibit 1** (2 pages) and a computer readable form of the Sequence Listing on a floppy disk is attached hereto. Pursuant to 37 C.F.R. §1.821(f), the Sequence Listing information recorded in computer readable form and filed herewith is identical to the paper copy of the Sequence Listing attached hereto as Exhibit 1.

Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this objection regarding sequence disclosures.

Rejections under 35 U.S.C. §112, First Paragraph

Claims 50-54 and 58-59 are rejected under the written description and enablement requirements of 35 U.S.C. §112, first paragraph. In this regard, the rejection appears to be based on a sentence in the specification that the Examiner interpreted as disclaiming or limiting applicants' invention solely to the use of exogenous DNA

encoding maxi-K and K_{ATP} for inducing relaxation of penile smooth muscle. Applicants respectfully traverse this rejection, and maintain that the specification provides a written description and an enabling disclosure for the claimed invention.

The application as filed provides a teaching of using gene therapy for regulating various smooth muscles including, for example, bladder smooth muscle cells, colonic smooth muscle cells, corporal smooth muscle cells, gastrointestinal smooth muscle cells, prostatic smooth muscle cells, or urethral smooth muscle cells (See, page 17, line 16 to page 18, line 7; Claim 4 as filed). In addition, the application as filed provides a teaching of using DNA encoding proteins that induce relaxation or contraction of smooth muscle including, for example, potassium channels, connexin 43, nitric oxide synthase, guanylate cyclase, adenylate cyclase, protein kinase G, protein A or calcium channels. (See, page 19, lines 10-17; page 20, lines 5-6; Claim 8 as filed).

With respect to relaxation of corporeal smooth muscle, the application as filed provides two specific examples of potassium channels, namely maxi-K and K_{ATP} , that can be introduced exogenously using gene therapy to induce relaxation of corporeal smooth muscle. However, applicants did not contemplate limiting their invention to the exclusive use of exogenous maxi-K and K_{ATP} . Rather, the specification is replete with numerous references to the use of exogenous potassium channels generally in connection with corporeal smooth muscle and for the treatment of erectile dysfunction. By way of example, the specification teaches at page 21, lines 11-21, that regulating penile smooth muscle includes the introduction and expression of a DNA encoding a protein involved in the regulation of smooth muscle tone, and at page 19, lines 10-17, page 20, lines 5-6,

and Claim 8 as filed, potassium channels are provided as examples of such proteins involved in the regulation of smooth muscle tone.

In addition, at page 27, lines 16-19, the specification teaches that “[p]otassium channels are important in the regulation of human smooth muscle tone” and that “[g]enes for more than thirty K⁺ channels, many of which are expressed in smooth muscle, have been identified.” The specification also teaches that the “existence of such a diverse repertoire of K⁺ channels has potentially-important implications for the modulation of electrical activity in human smooth muscle cells, including corporal myocytes.” (See, page 27, lines 21-24). With respect to the studies with maxi-K, the application states on page 68, line 19-21 that such studies “further document the importance of K⁺ channels in modulating corporal smooth muscle tone.” In the very next sentence, applicants also state “while it is recognized that there may be other subunits of the human smooth muscle maxi-K channel in human corporal tissue, these studies represent a reasonable starting point for evaluating the role of the maxi-K channel in erectile physiology.” (See, p. 68, lines 22-25). Similarly, the specification teaches at page 78, lines 23-27 in the context of erectile and bladder physiology that “[t]he goal of gene therapy is . . . to restore a more normal balance between contracting and relaxing stimuli following expression of (an) exogenous gene(s) that code(s) for physiologically-relevant proteins in smooth muscle (e.g., the maxi-K channel or K_{ATP}).” Clearly, applicants did not intend their invention to be limited to the exclusive use of exogenous maxi-K and K_{ATP}. Rather, applicants’ invention is to use exogenous potassium channels generally for inducing relaxation of corporeal smooth muscle. Accordingly, the Examiner’s reliance on the single sentence bridging pages 27-28 as a limitation on applicants’ invention is simply incorrect.

Applicants also note that the sentence bridging pages 27-28, even if read in isolation, was not meant to limit applicants' invention to maxi-K and K_{ATP} . That sentence is a discussion of the significance of maxi-K and K_{ATP} based upon an interpretation of prior art studies, and was not meant to limit the claimed invention to the use of maxi-K and K_{ATP} exclusively. The references cited at the end of the sentence, namely Dorschner, et al., Lee, et al. and Benevides, et al., were interpreted by applicants as prior art publications that presented evidence for the presence and physiological relevance of maxi-K and K_{ATP} in human corporal smooth muscle, despite the plethora of known potassium channel subtypes. However, the fact that applicants interpreted those publications as disclosing the presence and physiological relevance of maxi-K and K_{ATP} in human corporal smooth muscle does not mean, and should not be taken, as limiting the invention to maxi-K and K_{ATP} to the exclusion of other potassium channels. The passages referred to in the preceding paragraphs, as with other portions of the specification, clearly and unequivocally demonstrate that applicants contemplated the use of exogenous potassium channels generally for inducing relaxation of corporeal smooth muscle.

The application as filed also provides an enabling disclosure for using DNA encoding potassium channels for inducing relaxation of corporeal smooth muscle. In this regard, the application provides two working examples demonstrating that DNA encoding maxi-K and K_{ATP} , when introduced and expressed in corporeal smooth muscle, are capable of inducing relaxation of corporeal smooth muscle. The present application also teaches that "[g]enes for more than thirty K^+ channels, many of which are expressed

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in smooth muscle, have been identified.” (See, page 27, lines 16-19). Using the specific teachings of the application, including the teachings of the working examples with DNA encoding maxi-K and K_{ATP} , the skilled artisan could readily prepare and introduce DNA encoding a potassium channel of interest into a corporeal smooth muscle, and determine whether or not the expressed potassium channel induces relaxation of the corporeal smooth muscle, without undue experimentation. In the previous response, applicants provided evidence that two additional potassium channel proteins, namely, the voltage-dependent potassium channel protein Kv1.5 and the calcium-sensitive potassium channel protein SK3, when introduced and expressed in corporeal smooth muscle using techniques similar to those described in the application, are effective at inducing relaxation of corporeal smooth muscle. Based upon the examples in the specification and these experiments, applicants have now demonstrated that DNA encoding four potassium channels can be introduced and expressed in corporeal smooth muscle to achieve relaxation of corporeal smooth muscle. To require any more evidence is simple not required under U.S. patent law.

In summary, applicants maintain that the application as filed provides a written description and an enabling disclosure for the claimed invention. The sentence bridging pages 27 and 28 of the application is not a limitation of the invention to the use of maxi-K and K_{ATP} to the exclusion of other potassium channels. Rather, the application as filed teaches that applicants contemplated the use of potassium channels generally for enhancing relaxation of corporeal smooth muscle, and the application as filed provides an enabling disclosure for such use. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

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Information Disclosure Statement

An Information Disclosure Statement, including form PTO/SB/08A-B (2 pages), was submitted as part of applicants' response filed on May 20, 2003. Enclosed with the current Office Action was an initialized copy of the first page of the form (i.e., Form PTO/SB/08A), but not the second page (i.e., Form PTO/SB/08B). Applicants request that the Examiner initialize Form PTO/SB/08B submitted on May 20, 2003 to indicate that the references listed on the form have been considered and return a copy of initialized Form PTO/SB/08B to applicants.

Allowable Subject Matter

The Examiner indicated that claims 55-57 contain allowable subject matter, but are objected to as being dependent upon a rejected base claim. Applicants thank the Examiner for this indication of allowable subject matter, and respectfully request that the Examiner reconsider the allowability of all the pending claims in view of the remarks made hereinabove.

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CONCLUSIONS

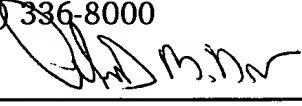
In view of the amendments and remarks made hereinabove, applicants respectfully request reconsideration and withdrawal of the objections and rejections set forth in the August 13, 2003 Office Action and passage of all of pending claims 50-59 to allowance. If there are any minor issues that would prevent allowance, applicants request that the Examiner contact the undersigned attorney.

No fee is deemed necessary in connection with the filing of this Amendment. However, if any fee is required to maintain the pendency of this application, the PTO is authorized to withdraw any such fee from Deposit Account 01-1785.

Respectfully submitted,

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